Rising Prostate Cancer Rates in South Korea

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BACKGROUND. Prostate cancer incidence and mortality rates in South Korea are relatively low, but rising steadily.
METHODS. We examined age-standardized incidence and mortality trends of prostate cancer in South Korea to gain further insight into prostate cancer etiology.
RESULTS. Although prostate cancer incidence has been low (7.9 per 100,000 man-years), it has increased up to 28.2% between 1996–1998 and 1999–2001. Prostate cancer mortality increased 12.7-fold over a 20-year period. Despite the increase in prostate cancer incidence and mortality rates, marked differences in rates remain for Koreans, Korean Americans, and Caucasian Americans.
CONCLUSIONS. The rising rates of prostate cancer in South Korea cannot be attributed entirely to PSA screening due to the low PSA screening prevalence; this trend is most likely related to increased westernization among Koreans. Interdisciplinary epidemiological studies incorporating the collection of biological samples are needed to clarify the extent to which lifestyle and genetic factors contribute to the observed racial disparity. *Prostate*
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INTRODUCTION

Prostate cancer is a very common cancer in Western populations. In the United States, prostate cancer is the most commonly diagnosed non-skin malignancy among men and is the second leading cause of cancer death, accounting for about 33% of all male cancer cases and 10% of all male cancer deaths [1]. In contrast, it is relatively uncommon in Asia. In South Korea, prostate cancer ranks as the eighth most common cancer among men, after cancers of the stomach, lung, liver, colorectum, esophagus, bladder, and pancreas [2]. Among men over the age of 65 years, it is the fifth most common cancer [2]. Prostate cancer accounts for 2.4% and 1.5%

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of the total cancer cases and deaths, respectively, among Korean men [2,3]. Despite the low rates, over the last few years, prostate cancer rates in South Korea, like in other Asian countries, appear to be rising steadily [4]. In this report, we examine recent trends for prostate cancer incidence and mortality in South Korea to uncover additional clues about prostate cancer etiology.

MATERIALS AND METHODS

Incidence

Cancer registration in South Korea began officially in 1980 with the creation of the Korea Central Cancer Registry (KCCR). By 2002, the KCCR registration system had expanded to include 131 hospitals, capturing 83,846 cancer cases from a population of more than 47 million residents [5]. Although participation of hospitals in the KCCR has been voluntary, the reporting of cancer cases has been fairly complete, with over 90% of all cancer patients reported to the KCCR since 1997 [2,5].

The first regional population-based cancer registry was formed in Kangwha County, a small rural island in South Korea, in 1983 [5]. Regional population-based cancer registries in nine regions were subsequently launched: Seoul (1991), Busan (1995), Daegu (1997), Kwangju (1997), Incheon (1998, incorporating Kangwha County), Daejeon (1999), Ulsan (2001), Jejudo (2001), and Goyang (2002) [5]. Case ascertainment in these regional registries has been over 96% [5], which is similar to the figure of 98% reported for the SEER registries [6].

Based on data collected by the KCCR, the eight regional cancer registries, and national death certification and health insurance programs, which together cover almost the entire population of South Korea [7], nationwide incidence of prostate cancer first became available for the period 1998–2000 [8]. Measures of several data validity indicators, including morphological verification of diagnosis (71.2–76.2%), death-certificate-only cases (7.4–7.5%), and mortality/incidence ratio (46.2–61.8%), suggest these reported data are of high quality [2].

For the time-trend analysis, we used age-standardized incidence rates for prostate cancer (ICD-9 Code 185; ICD-10 Code C61), directly age adjusted to the Segi world standard [9,10], for the three population-based regional cancer registries in South Korea, including Busan, Daegu, and Seoul (personal communication), reporting incidence data to the International Association for Research on Cancer (IARC) [10]. In addition, we acquired nationwide prostate cancer incidence for the period 1999–2001 [2]. For comparison of rates with other countries, prostate cancer rates from the US, Canada, and several countries in Asia, including Korea, were obtained from the IARC publication, *Cancer Incidence in Five Continents Volume VIII* [10].

Mortality

The national death certification data are also of high quality. It was estimated that about 99% of the total certified deaths in South Korea were classifiable and 95% of all deaths were confirmed by a physician's diagnosis in 2001. Before 1990, however, the proportion of deaths confirmed by a physician's diagnosis was much lower (66–75%) [3].

Based on national death certification data in South Korea, annual age-specific death rates for prostate cancer and the major cancers in South Korea were acquired from the Korea Statistical Information System (KOSIS) of the National Statistical Office in Korea [11] for the years 1983–2002. Prostate cancer rates for the United States were obtained from SEER statistics [12]. All mortality rates were age-adjusted to the Segi world standard population [9,10], using the direct method. The age group 80+ was an aggregate of the age groups 80–84, 85–89, 90–94, 95–99, and 100+.

RESULTS

Figure 1 shows the age-adjusted incidence of prostate cancer in the US, Canada, and several countries in Asia. The time period during which incidence has been reported for most countries was 1993–1997, although it was slightly different for a few countries. Prostate cancer incidence rates in Asian countries were much lower than those in Western countries. Within Asia, rates in South Korea exceeded only those in Vietnam and mainland China, where prostate cancer incidence has been among the lowest in the world. Korean rates were lower than those in most other Asian nations, including the Philippines, Singapore, Japan, Taiwan, Oman, and Hong Kong. Korean Americans have rates (22.0 per 100,000 man-years) that are about three times those of their counterparts in South Korea, although their rates remain substantially lower than those for US Whites and Blacks (107.8 and 185.4 per 100,000 man-years, respectively).

Table I shows the region-specific and nationwide age-adjusted incidence of prostate cancer in South Korea. According to the latest estimate (1999–2001), the nationwide incidence was 7.9 per 100,000 man-years, with regional rates ranging from 7.1 per 100,000 in Busan (the second largest city), to 7.3 per 100,000 in Daegu (the third-largest city), to 10.9 per 100,000 in Seoul (the capital). Although the reported rates have been relatively low, they have increased in most parts of South Korea. Specifically, rates rose 6.0%, 21.7%, and

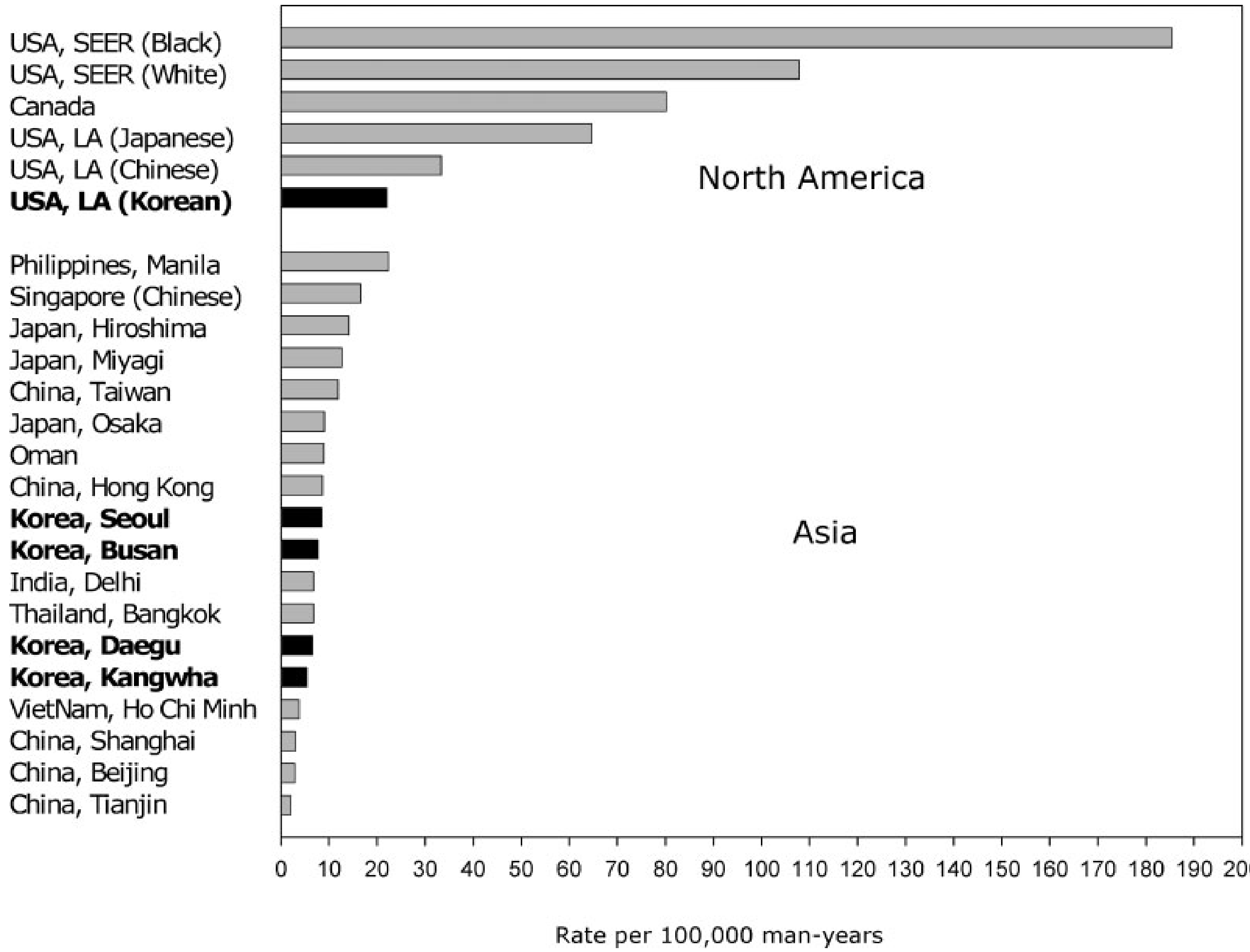

Fig. 1. Age-standardized incidence rates (1993 – 1997) for prostate cancer in South Korea, selected countries in Asia, and North America [10]. All incidence rates were age-adjusted to the Segi world standard population [9].

TABLE I. Age-standardized Incidence Rate (ASIR) per 100,000 Man-years for Prostate Cancer in South Korea

	Year	No. of cases	ASIR[a]	% increase
Nationwide incidence	99–01[b]	4,276	7.9	
Busan	93–95	—	—	—
	96–98[c]	196	6.7	—
	99–01[c]	258	7.1	6.0% (99–01 vs. 96–98)
Daegu	93–95	—	—	—
	97–98[d]	96	6.0	—
	99–01[d]	167	7.3	21.7% (99–01 vs. 97–98)
Seoul	93–95[e]	562	7.9	—
	96–98[e]	789	8.5	7.6% (96–98 vs. 93–95)
	99–01[e]	1,100	10.9	28.2% (99–01 vs. 96–98)

[a]Age-adjusted to the Segi world standard population [9].
[b]Korea National Cancer Center, 2005 [3].
[c]Busan Cancer Registry.
[d]Daegu Cancer Registry.
[e]Seoul Cancer Registry.

28.2% in Busan, Daegu, and Seoul, respectively, between 1996–1998 and 1999–2001.

Figure 2 shows the age-adjusted death rates for the major male cancers in South Korea, and for prostate cancer in the US, for the 20-year period from 1983 to 2002. Prostate cancer mortality rates in Korea rose 12.7-fold during this time period, from 0.30 to 3.82 per 100,000 man-years. In comparison, mortality rates for stomach cancer declined 50%, while those for lung and colorectal cancers increased by 3.5- and 4.9-fold, respectively, over the same time period. The US prostate cancer mortality rates increased slightly from 1983 to 1990, plateaued from 1990 to 1993, and declined thereafter.

DISCUSSION

Age-adjusted prostate cancer incidence and mortality rates in South Korea are much lower than those in most Western nations, but they have been rising steadily over time. Over the short period of time from 1996–1998 to 1999–2001, reported incidence rose by 28.2% in Seoul. From 1983 to 2002, mortality increased 12.7-fold nationwide, although the proportion of deaths confirmed by a physician's diagnosis before 1990 was much lower than in subsequent years. Similar increasing trends in prostate cancer incidence and mortality have been observed for other Asian countries, including China, Thailand, Hong Kong, Japan, and Singapore [4,13].

Although the sharp increase in prostate cancer incidence during the early 1990s in most Western populations has been attributed largely to PSA screening [14], it is unlikely that the rising incidence trends in South Korea can be explained entirely by increased PSA screening in this population. Population-based data on PSA screening are limited, since PSA screening in South Korea is not a common practice. According to a 2004 telephone survey of over 700 Korean men older than 50 years in a small city, approximately 15% had been screened for prostate cancer (PSA and digital rectal examination) during the previous 2 years (unpublished data), a much lower prevalence than the 75% reported for US men [15]. The observation [16] that prostate cancer diagnosis in Korea occurs at late stages with low survival further suggests that PSA screening is still relatively uncommon in South Korea. Although it is possible that improved diagnosis of prostate cancer in recent years could contribute to an increase in reported prostate cancer incidence [14], this effect is likely minimal, since there has been no major change in diagnostic criteria.

The steady rise in prostate cancer mortality in South Korea over time, both before and after the introduction of PSA screening, also supports the fact that the

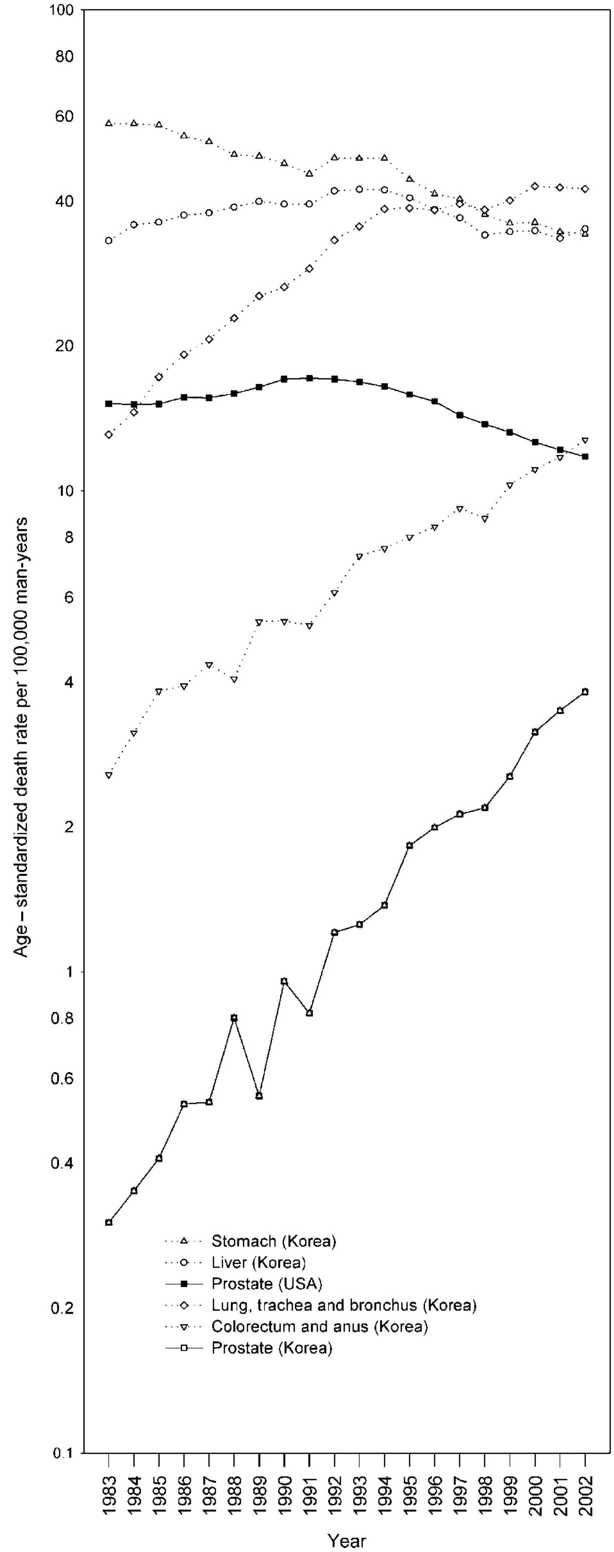

Fig. 2. Age-standardized death rates per 100,000 man-years for selected cancers among South Korean men and for prostate cancer among US men. Nationwide prostate cancer mortality rate increased 12.7-fold from 1983 to 2002 in Korea (0.30 to 3.82 per 100,000 man-years). All mortality rates [11,12] were age-adjusted to the Segi world standard population [9].

increase in incidence is not entirely due to prostate cancer screening. While increased screening can have a substantial impact on reported incidence, especially with respect to early-stage tumors, the impact on reported mortality is less clear. In fact, if PSA screening is effective in identifying early-stage tumors whose further development can be arrested, then it would eventually lead to a reduction in prostate cancer mortality. The fact that prostate cancer mortality rates in South Korea have increased steadily, even before the PSA screening era, further suggests that the parallel rise in both mortality and incidence is indeed real.

Reasons for the increases in prostate cancer incidence and mortality are unclear but may be explained in part by the gradual westernization of lifestyle in South Korea. Western lifestyle factors, such as increased meat and fat intake, have been linked to elevated prostate cancer risk [13]. The shift toward increased westernization in South Korea is evident from national survey data, such as the National Nutrition Surveys conducted between 1969 and 1995 and the National Health and Nutrition Surveys conducted every 3 years since 1998 [17–21]. Although the total caloric intake among men and women declined by 17.3%, from 2,390 kcal/day in 1975 to 1,976 kcal/day, in 2001, the composition of the Korean diet changed substantially (Table II), with a large increase in intake of animal foods. Specifically, during this time period, daily intake of meat and meat products increased 5.4-fold (from 14.3 to 91.7 g) [17–19]. As a result, the percent of calories from fat increased 1.3-fold (from 8.6% to 19.5%), the percent of fat intake from meat and meat products increased 3.7-fold (from 6.0% to 28.4%), and the percent of protein intake from animal sources rose 8.5-fold (from 2.3% to 21.8%) [17–19]. In contrast, intake of cereals and grains as well as potatoes and starch decreased more than 25%. From 1995 to 2001, the prevalence of being overweight (BMI 25.0–29.9) in South Korea rose from 18.0% to 30.1%, and that of obesity (BMI $\geq$30) from 0.8% to 2.2%; the prevalence of central adiposity (waist circumference $\geq$90 cm) also increased from 9.2% to 25.2% [20,21]. While energy imbalance is an important factor in westernization, and perhaps prostate cancer, it appears that in South Korea, changes in dietary composition are a more likely explanation for the recent rise in prostate cancer rates, given that the proportion of Korean men engaging in intermittent low or regular moderate exercise has changed little in recent years (32.6% in 1998 to 31.7% in 2001) [22].

The observed regional variation in prostate cancer incidence, along with dietary patterns, in South Korea further supports our westernization hypothesis. Prostate cancer incidence in Seoul, the largest and presumably the most westernized city, has been higher than that in Busan and Daegu, the second and third largest cities. In contrast to these three cities, incidence in Kangwha, one of the more rural regions, has been much lower (5.4 per 100,000 in 1993–1997) [10]. Differences in dietary patterns between urban and rural areas of South Korea may also reflect the increased westernization in urban areas. Residents of urban areas consume more total calories (2002 vs. 1883 kcal/day) and animal fat (21.2 vs. 15.0 g/day) and have a higher percentage of calories from fat (20.1% vs. 16.6%) than residents of rural areas [18].

Despite the increasing prostate cancer incidence and mortality rates in South Korea, marked differences remain between the rates for Korean versus US men. Reasons for these disparities are unclear but may be related to differences in the prevalence of putative risk factors for prostate cancer, including dietary fat intake

TABLE II. Daily Dietary Intake of South Koreans in 1975 and 2001

	1975[a,b]	2001[c]	% change
Energy (kcal/day)	2,390	1,976	−17.3
Meat, poultry, and their products (g)	14.3	91.7	541.3
Cereals and grain (g)	473.8	310.5	−34.5
Potatoes and starch (g)	35.8	26.5	−26.0
Vegetables (g)	245.7	290.8	18.4
Fruits (g)	22.4	207.4	825.9
% calories from fat	8.6	19.5	126.7
% calories from protein	12.8	14.9	16.4
% of fat intake from meat and meat products	6.0	28.4	373.4
% of protein intake from meat and meat products	2.3	21.8	847.8

[a]1975 National Health and Nutrition Survey [17].
[b]Kim SW et al., 2001 [19].
[c]2001 National Health and Nutrition Survey [18].

and obesity. Korean men consume fewer total calories per day (2,335 kcal) relative to US men (2,475 kcal), with a pronounced difference in caloric intake from fat (18.8% for Korean men vs. 33% for US men) [19,23]. However, the intake of vegetables and fruit, which has been linked to reduced prostate cancer risk in numerous studies [24–26], is slightly lower among men living in Korea than in the US (400 g/day in Korean men vs. 444 g/day in US men during 1980–1987) [27,28]. Korean men also have a much lower mean BMI (23.7 kg/m^2 in 2001 vs. US White 27.9 kg/m^2 and US Black 27.5 kg/m^2 in 1999–2002) [21,29]. Similarly, the prevalence of obesity (BMI $\geq$30) in Korea has been substantially lower than that in the US (2.2% vs. 30%) [21,30]. Also, Korean men have a smaller mean waist circumference of 82.9 cm (1998), compared to 96.3 and 91.8 cm (1988–1994) for US White and Black men, respectively [21,31].

Another possible explanation for the large difference in prostate cancer risk between Korean and Western men is racial differences in androgen metabolism or other biological factors related to prostate carcinogenesis. For example, it has been suggested that Asian men have lower levels of circulating androgens and less active intraprostatic 5-alpha-reductase activity, resulting in lower androgenic activity within the prostate gland and lower prostate cancer risk [32–34]. It has also been suggested that differences in the prevalence of polymorphisms in the *SRD5A2* gene (AT and TT genotypes of *SRD5A2* A49T; VL and VV genotypes of *SRD5A2* V89L), hypothesized to be associated with prostate cancer risk [32–34], may help explain the racial difference in prostate cancer incidence. Data on serum hormones and genetic polymorphisms related to prostate cancer among Korean men are limited. However, in two recent studies, the prevalences of the risk alleles for the *SRD5A2* A49T and V89L markers among Korean men (1% and 71%, respectively) were lower than among Caucasian men (3–6% and 87–95%, respectively) [35,36].

CONCLUSIONS

Population-based data from South Korea suggest that prostate cancer incidence and mortality rates remain low but have been increasing steadily for two decades. This upward trend may be explained in part by increased westernization, including greater intake of animal-derived foods and increased prevalence of overall and abdominal obesity, and, to a smaller extent, by increased PSA screening. Nevertheless, a major part of the disparity in prostate cancer incidence between men in Korea and the United States remains unexplained. Future high-quality studies with large sample sizes and individual-level exposure and molecular assessments are needed to provide insight into the role of putative risk factors, which will help elucidate both independent and combined effects of environmental and genetic factors in prostate cancer etiology and uncover reasons for the racial differences in prostate cancer risk.

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